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Lipid Profile Changes in Children with Acute Lymphoblastic Leukemia

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Abstract: Background: Abnormal lipid profile has been associated with cancers, including acute lymphoblastic leukemia ALL, the most common form of malignant disease in the paediatric age group; also, drugs used in induction therapy affects the lipid profile. Objective: The objective of this study was to investigate the frequency of altered lipid profiles in children with (ALL) at diagnosis and after induction therapy. Patients and methods: Fasting lipid profile (s. cholesterol, sTG, HDL-C, LDL-C) for about 10-12 hours has been obtained from each patient In this case-control study. Lipid profiles of 26 cases with newly diagnosed ALL (13 males and 13 females) were compared with those of 40 healthy controls (20 males and 20 females) of the same age and gender from the 1st of February to the 31st of October 2010, then we compare lipid profile readings of 21 ALL with lipid profile readings of the same patients after completion induction therapy (we excluded 5 ALL cases who died before starting induction therapy). Results: The lipid profiles in the newly diagnosed ALL patients at diagnosis showed the following values: s.cholesterol 153.8±41 mg/dl, sTG 176.8±97.9mg/dl, HDL-C 38.5±15.5mg/dl, and LDL-C 88.3±41.5 mg/dl, the lipid profiles after induction therapy showed s.cholesterol 168.5±51.6 mg/dl, sTG 212.1±100.25mg/dl, HDL-C32.1±14.05mg/dl and LDL-C 104.4±41.34mg/dl, whereas for controls they were 144.02±22.9mg/dl, 106.8±48.8mg/dl, 34.1± 7.3mg/dl, 88.9±27.2mg/dl respectively. Abnormalities in lipid profiles regarding s TG showed that it was significantly higher in newly diagnosed ALL in comparism to controls, while s. cholesterol and HDL-C were higher among the patients, but it was statistically not significant, and LDL-C seems to be similar or slightly higher than controls, but they were not significant. Results showed that there were significant elevations in sTG and LDL-C in the patients after induction therapy compared to a diagnosis, whereas there was a significant reduction in HDL-C after induction therapy compared to the readings at diagnosis. Conclusion It can be concluded from this study that at the moment of diagnosis, a change in lipid profile could be established and might be atherogenic. And these changes include a significant elevation of s TG, and while other changes like s. cholesterol and HDL elevations were not significant statistically. Lipid profile alteration presents specifically during combination therapy of 1-asparaginase and steroids in induction therapy in ALL patients, which includes further elevations of s TG, LDL, and reduced HDL, and as we know that, these changes might be atherogenic.

Keywords: Lymphoblastic Leukemia, HDL-C, LDL-C, ALL

INTRODUCTION

Acute lymphoblastic leukemia (ALL) is a type of cancer that primarily affects children. It is important to monitor lipid profile changes in children with ALL due to the potential impact on overall health and treatment outcomes [Morel, S. *et al.*, 2017; Mohapatra, S. *et al.*, 2016].

Research suggests that lipid profile changes occur in children with ALL, although the specific alterations may vary among individuals. Some common lipid profile changes observed in children with ALL include:

Increased total cholesterol: ALL treatment, including chemotherapy and corticosteroids, may result in elevated total cholesterol levels. This increase is linked to the drugs' effect on lipid metabolism [Bhojwani, D. *et al.*, 2014; Moschovi, M. *et al.*, 2004].

Elevated triglyceride levels: Triglyceride levels tend to be higher in children with ALL, possibly due to the disease itself or as a side effect of chemotherapy. Elevated triglycerides can increase the risk of cardiovascular disease [Zalewska-Szewczyk, B. et al., 2008; Cohen, H. et al., 2010].

Changes in high-density lipoprotein (HDL) cholesterol: HDL cholesterol, often referred to as "good cholesterol," may decrease in children with ALL. Reduced HDL levels could be a result of treatment-induced alterations in lipid metabolism.

Altered low-density lipoprotein (LDL) cholesterol: The impact of ALL on LDL cholesterol is less clear. Some studies suggest that LDL cholesterol levels may increase, while others report no significant changes [Finch, E. R. *et al.*, 2020].

Disruptions in lipid profiles during treatment: Lipid profile changes often fluctuate during different phases of ALL treatments. For example, certain chemotherapeutic agents can cause acute lipid profile alterations, which may return to nearnormal levels during maintenance therapy [Shokunbi, W. A. *et al.*, 1991; Parsons, S. K. *et al.*, 1997].

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Monitoring and managing lipid profile changes in children with ALL is crucial for several reasons. Firstly, abnormal lipid levels may contribute to the development of cardiovascular diseases later in life. Secondly, lipid alterations may impact treatment outcomes, such as drug efficacy and toxicity [Friedewald, W. T. *et al.*, 1972; Friberger, P. *et al.*, 1978].

Regular lipid profile assessments, along with appropriate interventions if needed, can help minimize the potential long-term health risks associated with lipid profile changes in children with ALL. It is recommended to work closely with healthcare professionals to monitor and manage any alterations in lipid levels during and after treatment [Hamill, P. V. *et al.*, 1979; National Cholesterol Education Program, 1987; Ortega, J. A. *et al.*, 1977].

Regular lipid profile assessments, along with appropriate interventions if needed, can help minimize the potential long-term health risks associated with lipid profile changes in children with ALL. It is recommended to work closely with healthcare professionals to monitor and manage any alterations in lipid levels during and after treatment [Sallan, S.E. *et al.*, 1978; Steinherz, P. G. *et al.*, 1994].

This study aims to:

1- To assess blood lipid profile in newly diagnosed patients with ALL.

2-the alterations in the blood lipid profile after induction therapy.

PATIENTS AND METHODS

The study setting:

The present study was carried out in Nanakaly Hospital, which is the only hospital in Erbil City for Hematology and oncology, receiving patients from different administrative areas.

The study design: -

Case-control study was adopted to achieve the purpose of the study.

Duration of the Collection of Data of Study

The study was conducted in a period of eight months, from the beginning of February 2010 to the 29th of September 2010.

Selection of the Study Participants

Twenty-six newly diagnosed ALL children under 14 years of age who were attend Nanakaly Hospital in Erbil Governorate during the study period had been enrolled in this study. A group of controls matched for age and gender had been selected from the kinder garden, schools, and those who attend the outpatient clinic for simple purposes by simple random sampling in Erbil city.

Cases of hypothyroidism, nephrotic syndrome, familial hypercholesterolemia, DM, and those receiving medications will be excluding from the study.

The Data Collection

A questionnaire was designed by the researcher (Appendix 1). Information will be collected from the parents of the participants via a face-to-face interview and include age, gender, and residence, duration of illness, family history, and Protocol used in treatment. Written consent be will take from the parents of each child who will enroll in this study.

Investigation:

Blood lipid profile (S. cholesterol, HDL-C, LDL-C, S. triglycerides) and venous blood sample were obtained after 10-12 hours of fasting by taking a few ml of blood by venepuncture using plain tubes (we took one sample from each member of the healthy controls and two separated samples from the ALL patients the first at the diagnosis of ALL and the second after the completion of the induction therapy)

After that, the serum was separated within 30 minutes by centrifugation using HITACHI centrifuge for 10 minutes, then processed immediately for measuring serum cholesterol, serum TGs, HDL-C, then LDL-C was derived by Fredrickson- Friedwald formula [LDL-C=(TC-HDL)-TG/5].

Limitations

The sample size which was relatively small and might affect the results.

There is difficulty in taking a fasting blood sample from both the patients and controls, and we face other problems like clotting of blood samples, which need repetition, also hemolysis of the samples of the blood.

Data Analysis

Data will be entering into the Statistical Package for Social Science (SPSS) program for Windows version 18.

RESULTS

The age group and gender of patients and controls are distributed as shown below in Table 1.

Table 1: Age and gender distribution of patients and control								
	Age and Gender	Patients No. and %	Controls No. and %					
	1-7 years	18 (69.2%)	25 (62.5%)					
	8-14 years	8 (30.8%)	15 (37.5%)					
	male	13 (50%)	20 (50%)					
	Female	13 (50%)	20 (50%)					

Regarding the newly diagnosed ALL patients, those with age group 1-7 years represent 69.2% of all the cases while those with age group 8-14 years represent 30.8% of the sample of the patients, but regarding the controls those with age group 1-7

years represents 62.5% of them and those with age group 8-14 years represents 37.5%.

Regarding gender distribution of both the patients and the healthy controls, males represented by 50% and females represented also by the same percent.

Table 2: Lipid profile in controls and ALL patients						
	ALL Patients*	Control**				
Variables	Mean±SD	Mean±SD	P-value			
S. cholesterol (mg/dl)	153.8±41.04	144.02±22.9	0.220			
S. TGs (mg/dl)	176.8±97.9	106.8 ± 48.8	0.002			
HDL-C (mg/dl)	38.5±15.5	34.1±7.3	0.125			
LDL-C (mg/dl)	88.3±41.5	88.9±27.2	0.450			

*Total number of ALL patients is 26.

** Total number of controls is 40.

Despite the mean fasting s. cholesterol and HDL-C were higher among the patients with ALL compared with controls. These results with no significant relationship, and also, despite the mean fasting LDL-C was lower among ALL patients compared with controls, the results were of no significance, as shown in Table 2.

The mean fasting s.TG was significantly higher among ALL patients compared with controls, as shown in Table 2.

Variables	Newly diagnosed ALL*	Patients after induction*	P-value
	Mean±SD	Mean±SD	
S. cholesterol (mg/dl)	156.9±43.4	168.5±51.6	0.38
S. TGs (mg/dl)	157.9±98.5	212.1±100.25	0.028
HDL-C (mg/dl)	40.9±14.7	32.1±14.05	0.034
LDL-C (mg/dl)	81.7±36.5	104.4±41.34	0.039

*Total number of ALL patients at diagnosis & after induction is 21.

The mean fasting s.TG and LDL-C were significantly higher in ALL patients after receiving induction therapy compared with the same patients at diagnosis before starting chemotherapy.

The mean fasting HDL-C was significantly lower among ALL patients after completing induction

therapy compared with the same patients at diagnosis before receiving treatment.

In spite of higher levels of mean fasting s. Cholesterol in the patients after induction therapy compared with the same patients before therapy, the relationship of no significances.



Figure 1: Relation between healthy children's lipid profiles and newly diagnosed ALL patients



Figure 2: Lipid profile changes in ALL patients after completion of induction therapy compared with the same patients at diagnosis

DISCUSSION

Abnormal blood lipid profiles have been associated with cancer. The objective of this study was to investigate the frequency and of altered lipid profiles in children with acute lymphoblastic leukemia (ALL), the most common form of malignant disease in this age group.

In our study, we found that there were changes in the lipid profile have been seen in the newly diagnosed cases ALL, and these changes might be related to the disease itself, like a highly significant elevation of s.TG. As the lipids may be a biomarker of Steroid and Lasparaginase effects so, we also found significant lipid profile changes in 21 patients taking lasparaginase and steroids compared statistically with the same group of patients after excluding five dead cases results, who were passed before starting induction therapy, these results include significant elevations in both s.TG and LDL and a significant decrease in HDL-C after completing induction therapy, and it is important to take these changes in consideration because these changes may provide insight into toxicity associated with these drugs in addition to morbid and lethal effects of abnormal elevation of sTG and LDL that indicate atherogenisity.

In this study, mean fasting s. cholesterol and HDL-C were higher in newly diagnosed ALL patients than controls, although the difference was not significant statistically, and this is inconsistent with other studies done by Naik, *et al.*, done in India [2006] and Halton, *et al.*, done in Canada [2000] and Zalewska-Szewczyk, *et al.*, 2008 done in Poland. Which were showing reduced s. cholesterol and HDL-C in ALL patients compared with the controls and may attributed to the small sample size in our study.

In the present study, we notice that there is a raised mean fasting s.TG which was statistically significant (p-value=0.002) in newly diagnosed cases ALL when compared with controls, our study results are in agreement with other studies, Naik, *et al.*, done India [2006] Halton *et al.*, done in Canada and Zalewska-Szewczyk, *et al.*, done in Poland ⁽⁴¹⁾ which were showing elevated s.TG in newly diagnosed ALL patients compared with controls.

These changes in lipid profile in newly diagnosed ALL might be due to altered lipid metabolism or nutritional states.

In our study, there is a neglected rising statistically in LDL-C in newly diagnosed ALL patients comparing with controls, and this is inconsistent with other studies done by Naik *et al.*, Done in India ⁽³⁹⁾, Halton, *et al.*, 2000 done in Canada, and Zalewska-Szewczyk, *et al.*, 2008, done in Poland.

In this part of our study, we compare statistically lipid profiles in 21 cases of ALL patients before starting treatment with the same patients after completion of induction therapy with the exclusion of 5 patients results who were passed before starting or completion of induction therapy; we found that there was significant (statistically) elevation of sTG and LDL and significant reduction in HDL in the patients and these changes suggests L-asparaginase specific alterations and may provide insight into the toxicity associated with this drug in addition to steroid given during this phase of treatment.

In our study, the mean fasting s. cholesterol was raised in ALL patients after completion of induction therapy in comparism with the same patient's results at diagnosis, although it is statistically not significant. The latter results were in agreement with other study done by Kohen, H. *et al.*, ⁽⁴²⁾ and Zalewska-Szewczyk, *et al.*, done in Poland [2008]

In the present study, the mean fasting s.TG was raised in ALL patients receiving induction therapy, and the results were statistically significant compared with the results in the same patients at the time of diagnosis. And all these were in agreement with results in other study done by Halton, J.M. *et al.*, done in Canada [Halton, J. M. *et al.*, 2000] Zalewska -Szewczyk *et al.*, done in Poland ⁽⁴¹⁾, and Kohen *et al.*, study

Also, in our study, the mean fasting HDL-C decreased in ALL patients receiving induction therapy, and the results were statistically significant compared with the results in the same patients at the time of diagnosis. And all these results were in agreement with results in other study done by Halton JM et al., done in Canada [Halton, J. M. et al., 2000]. In our study, the mean fasting LDL-C in ALL patients receiving induction therapy Comparing with the results in the same patients at the time of diagnosis was elevated and statistically significant (p- value= 0.039), these results were inconsistent with other study done by Halton JM et al done. In Canada (40), and these results were in agreement with other study done by Zalewska-Szewczyk et al., done in Poland[;] these lipid profile changes (hyperlipidemia) occurred during induction therapy in ALL patients that includes combination therapy of L-asparaginase and steroids (the last drug. cause increase TG synthesis, and the former inhibits LPL activity) These two effects mean that the TG-rich lipoproteins are rapidly formed and insufficiently removed ⁽²⁵⁾.

CONCLUSIONS

It can be concluded from this study that at the moment of diagnosis of ALL, a change in lipid profile could be established, and these changes include a significant elevation of s TG and other changes like s. cholesterol and LDL elevation, although the latter changes were not significant statistically.

There is also specific lipid profile alteration during combination therapy of l-asparaginase and steroids during induction therapy in ALL patients that resemble results of other studies, which include further elevation of s TG, LDL, and reduced HDL, and as we know that, these changes are usually atherogenic.

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